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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,123	08/13/2001	Joseph M. Kinkade Jr	68-97	8722

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EXAMINER
COOK, LISA V

ART UNIT	PAPER NUMBER
1641	

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/831,123	Applicant(s) KINKADE JR ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *45-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-44* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☒ Claim(s) *1-81* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8 & 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' election of Group I – claims 1-44 (Paper#13 filed 5/8/03) with traverse is acknowledged. Applicant does not traverse the Restriction Requirement on the grounds of lack of patentable distinctness.

I. The traversal on the ground(s) "that unity of invention was found in accordance with PCT Rule 13.1 and 13.2 has been carefully considered but not found persuasive because the Examiner is not bound by the PCT prosecution but National stage requirements.

Please see 37 CFR 1.141. Different inventions in one national application.

(a) Two or more independent and distinct inventions may not be claimed in one national application, ex-cept that more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim gen-eric to all the claimed species and all the claims to species in excess of one are written in dependent form (§ 1.75) or otherwise include all the limitations of the generic claim.

(b) Where claims to all three categories, product, process of making, and process of use, are included in a national application, a three way requirement for restriction can only be made where the process of making is distinct from the product. If the process of making and the product are not distinct, the process of using may be joined with the claims directed to the product and the process of making the product even though a showing of distinctness between the product and process of using the product can be made.

II. The traversal on the ground(s) "that the special technical feature is the biomarker of oxidative stress, not the antibodies has been carefully considered but not found persuasive because biomarkers for oxidative stress as recited in the instant claims is not special.

The special technical feature (biomarkers for oxidative stress) that appears to link claims 1-81 does not provide a contribution over the prior art. The abstract to Papp et al., ORVOSI HETILAP, 1/26/97, 138(4), pages 201-205 disclose the inventive biomarkers for oxidative stress (sulfur containing amino acids methionine, cysteine, and selenium). Therefore the technical feature recited in claims 1-81 is not a contribution over the prior art. Accordingly the groups set forth below are not so linked as to form a single general concept under PCT Rule 13.1.
do not relate to a single general inventive concept under PCT Rule 13.1 or under PCT Rule 13.2.

2. The Restriction Requirement is still deemed proper and is therefore made **FINAL.**

3. Currently, claims 1-81 are subject to Restriction and Election Requirement. Claims 45-81 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as claims drawn to a non-elected invention. Claims 1-44 are currently under examination.

Priority

4. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application (PCT/US99/26133 filed 11/5/99), specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. Please add to the disclosure.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

6. The information disclosure statements filed 7/2/02 in paper #8 and 1/3/03 in paper #10 have been considered as to the merits before First Action.

Drawings

7. This application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

9. Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically Claim 1 is directed to method of detecting a biomarker of oxidative stress while claim 17 is a substantial duplicate reciting detection by any method. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 1-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 1-44 the use of "antigen binding fragment thereof" is indefinite. It is apparent that the antibody produced from hybridoma cell line KF2.F1 is required to practice the claimed invention. However the possession of the antibody does not provide sufficient meaning with respect to the infinite antigens with which the antibody may bind. It is suggested that "antigen binding fragment thereof" be eliminated from the claims in order to obviate this rejection.

B. Claims 1, 23, 37, and 41 are indefinite in their recitation as methods because the methods do not clearly set forth method steps and there is an absence of a resolution step, which reads back on the preamble of the claimed methods.

C. Claims 9, 10, 14, 15, 30, 31, 34, and 35 recite the limitations of "specific and non specific". The intended limitations refer to antibody compositions, however this is vague and indefinite because it is not clear as to what protein the antibodies are specific or non specific for. Is it applicants intent to mean the antibodies are specific and non specific for any and all proteins? As recited the metes and bound of the claims cannot be determined. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth monoclonal antibodies produced from the hybridoma cell line KF2.F1 (see pages 17 and 48) and therefore the written description is not commensurate in scope with the claims drawn to the utility of any antibody or binding fragment thereof.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117).

The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of hybridoma KF2.F1 (PTA-897), the skilled artisan cannot envision the detailed structure of the encompassed all possible antibodies/binding fragments thereof and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The monoclonal/polyclonal antibody itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of a compound/seq.id/etc. by only their functional activity does not provide an adequate written description of the genus.

The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules, usually defined by a sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, no disclosure, beyond the hybridoma KF2.F1 (PTA-897) is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only the isolated antibodies produced via hybridoma KF2.F1 (PTA-897), but not any antibody or antigen binding fragment thereof would meet the full breadth of the claims as required by the written description provision of 35 USC 112, first paragraph.

12. Claims 1-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for the method employing an antibody or antigen binding fragment thereof for binding a biomarker of oxidative stress because the instant specification is not in compliance with the biological deposit rules. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation.

Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims. The invention is a method to detect biomarkers of oxidative stress using an antibody or antigen-binding fragment thereof. According to prior art references, antibodies can be readily produced; however, the total characterization of an antibody is a long and complex procedure, which varies widely with the intended use of the antibody. A general point is that if a single hybridoma has been produced and is intended for a specific function it is unlikely that the antibody produced will have all the required characteristics (Campbell, Laboratory Techniques, Vol. 13, 1984). Campbell teaches that it is a waste of both reagents and time to attempt full characterization of an antibody, which is not obtained from a fully cloned cell line. See Chapter 10, specifically page 186. While the specification provides enough information for one of ordinary skill in the art to produce hybridoma cell lines secreting antibodies with the same or similar properties as the antibodies produced from KF2.F1, reproduction of an identical cell line and antibody is an extremely unpredictable event (see Campbell above), and because the specification lacks complete deposit information for the deposit of the hybridoma cell line(s) secreting the antibodies or antigen-binding fragments thereof, it does not appear that antibodies are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because certain of the claims specifically require the use of monoclonal/polyclonal antibodies or antigen-binding fragments thereof, a suitable deposit of the hybridoma cell lines for patent purpose is required.

In the case of hybridoma cell line K2.F1.6 (PTA-897) on page 48 of the disclosure, it appears that a deposit was made and a ATCC accession number may be applicable; however, no ATCC number is included in the specification and the requirements that the deposit was made under the provisions of the Budapest Treaty is not included.

If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when a deposit is made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and address of the depository is required.

Furthermore, unless the deposit was made at or before the time of filing, a declaration filed under 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know should identify the deposited monoclonal antibody or cell line by its depository accession number established the deposited antibody or cell line is the same as that described in the specification, and establish that the deposited antibody or cell line was in applicant's possession at the time of filing, In re Lundak, 27 USPQ90.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

I. Claims 1-2, 8-10, 13-15, 17, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Osawa (Shipin Kexue Taipei, 24(6), Abstract Only, 1997).

Osawa teaches methods of assessing lipid hydroxyperoxides and secondary products of oxidative breakdown in numerous plant materials. The reaction products are important biomarkers for antioxidative activity of dietary antioxidants. Specifically the reference employs monoclonal and polyclonal antibodies in immunochemical detection methods to measure the antioxidants.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 3-7, 11-12, 16, 18-19, and 21-44 are rejected 35 U.S.C. 103(a) as being unpatentable over Osawa (Shipin Kexue Taipei, 24(6), Abstract Only, 1997) in view of Ding et al. (Journal of Biochemistry, 1998, 332, pages 251-255) and in further view of Roberts et al. (US Patent #5,700,654).

Please see Osawa as set forth above.

Oswawa differs from the instant invention in not specifically teaching an antibody specific for oxidized sulfur or selenium containing amino acid compositions.

However, Ding et al. teach an antibody which detects selenium. The selenium containing catalytic antibody Se-4A4 The antibody binding characteristics are useful in monitoring free radical activity (damage and protection). See abstract and pages 251 Introduction. The antibodies were produced in mice and tested in an ELISA protocol. Pages 251-252.

Although Ding et al. are silent with respect to the catalytic activity being oxidation, Roberts et al. teach the importance of oxidation state in the assessment of oxidation stress. Roberts et al. teach methods of assessing oxidative stress by quantifying prostaglandin F_2 like compounds and their metabolites. The metabolites are produced by noncyclooxygenase free radicals. These radicals include oxidized products from sulfur containing proteins (methionine sulfoxide from methionine). Column 1 lines 51-52.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an antibody that binds oxidized sulfur or selenium containing amino acids as taught by Ding et al. in view of Roberts et al. in the oxidative breakdown process of Osawa because Ding et al. teach that the antibodies against selenium was useful in evaluating oxidative damage and protection (page 251) while, Roberts disclosed that the oxidative state is further crucial in the oxidative measurements (column 1).

One of ordinary skill in the art would have been motivated to include an antibody to measure selenium in order to take advantage of antibody specific binding and further measure the oxidation state in order to more precisely understand oxidation as it relates to oxidative stress.

15. For reasons aforementioned, no claims are allowed.

Remarks

16. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Papp et al. (ORVOSI HETILAP, 1/26/97, 138(4) PAGES 201-205) disclose methods of assessing oxidative stress via free sulfhydril groups in plasma, and the blood selenium levels.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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7/25/03

LONG V. LE
SUPERVISORY PATENT EXAMINER
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07/28/03